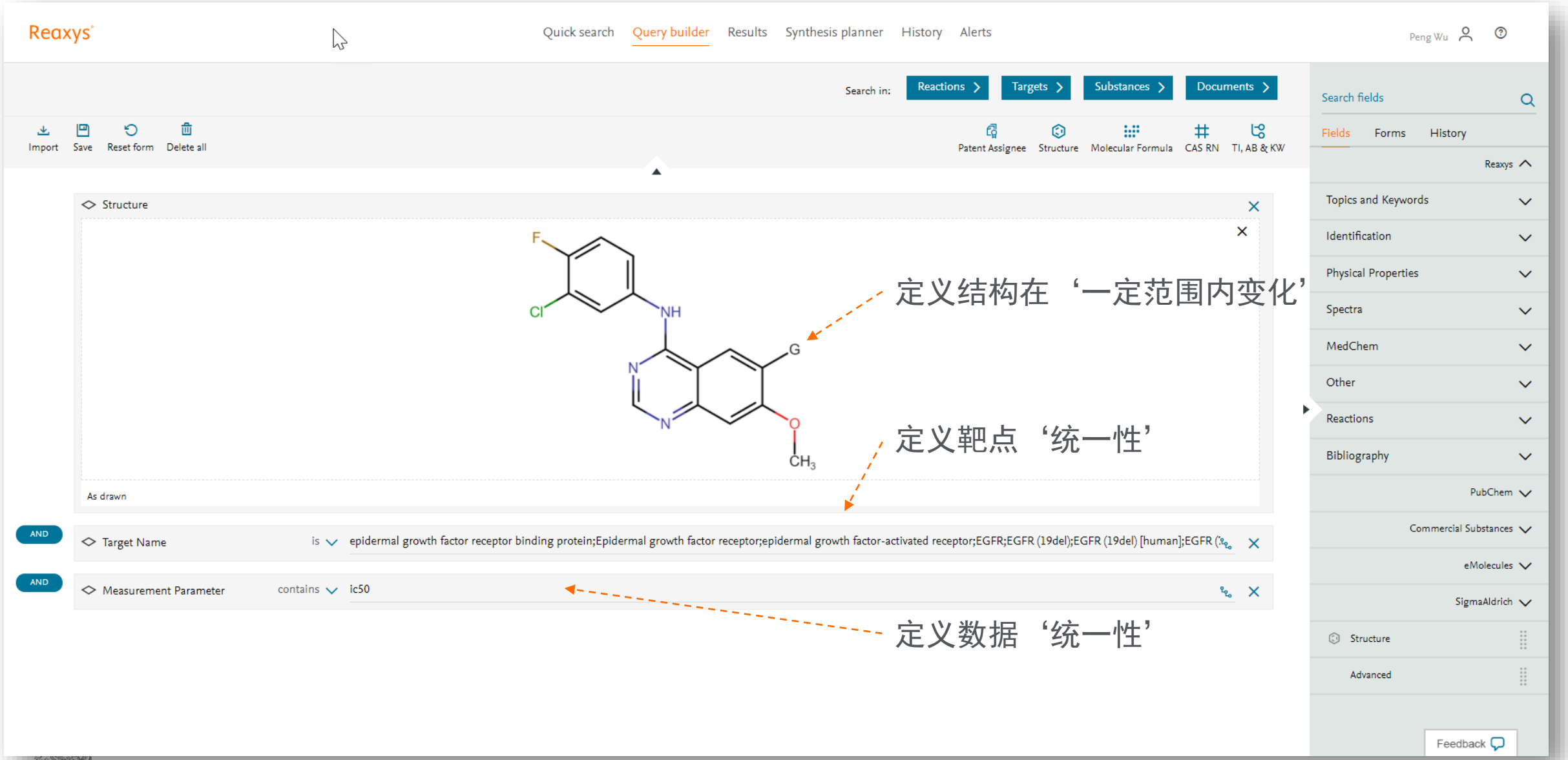
Elsevier Life Science Solution

Reaxys药化数据应用

吴鹏 16621600327
p.wu.1@elsevier.com
爱思唯尔生命科学客户顾问

Reaxys药化数据检索-IC50



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对于数据库的整理

1. 对设定参数数据单独进行展示

2. 对数据进行标准化

数量级标准化
统一到摩尔

原始数据标注

细胞系标注

测试试剂标注

436 Substances out of 353 Documents, containing 1,352 Reactions, 97 Targets

0 selected | Limit To | Exclude | Export | Preparations

1 **gefitinib**
$C_{22}H_{24}N_4ClFO_3$ 446.909 8949523 184475-35-2
Identification
Druglikeness
Bioactivity (Hit Data)

2 **4-(3-chloro-4-fluorophenylamino)-6-hydroxy-7**
$C_{15}H_{11}ClFN_3O_2$ 319.723 8928756 184475-71-6
Identification
Druglikeness

3 **Dacomitinib**
$C_{24}H_{25}ClFN_5O_2$ 469.946 12400147
Identification
Druglikeness

400+跨文献的改构化合物
数据统一标准化

Quantitative Results

pX	Parameter	Value (qual)	Value (quant)	Unit	Biological Species	Action on target	Target	Cell	Bioassay	Dose	Effect	Concomitants
10	IC50		0.1	nM			Epidermal growth factor receptor [human]:Wild	Baculovirus-infected insect cell	Enzymology inhibition			CoEnzyme: ATP; Solvent: DMSO;
10	IC50	=	0.1	nM	human	Inhibitor	Epidermal growth factor receptor [human]:Wild	NCI-H3255 cell line				
10	IC50		0.0001	μM			Epidermal growth factor receptor [human]:Wild		Enzymology inhibition	5.10000E-09 M		CoEnzyme: ATP; Solvent: DMSO;
10	IC50		0.0001	μM			Epidermal growth factor receptor:Wild		Enzymology inhibition			CoEnzyme: ATP; Solvent: DMSO;
10	IC50	=	0.0001	μM		Inhibitor	Epidermal growth factor receptor:Wild					
9.82	IC50		0.15	nM		Inhibitor	Epidermal growth factor receptor [human]:Wild					
9.77	IC50		0.17	nM		Inhibitor	Epidermal growth factor receptor [human]:Mutated					

Show Less

数据导出后可以二次删选

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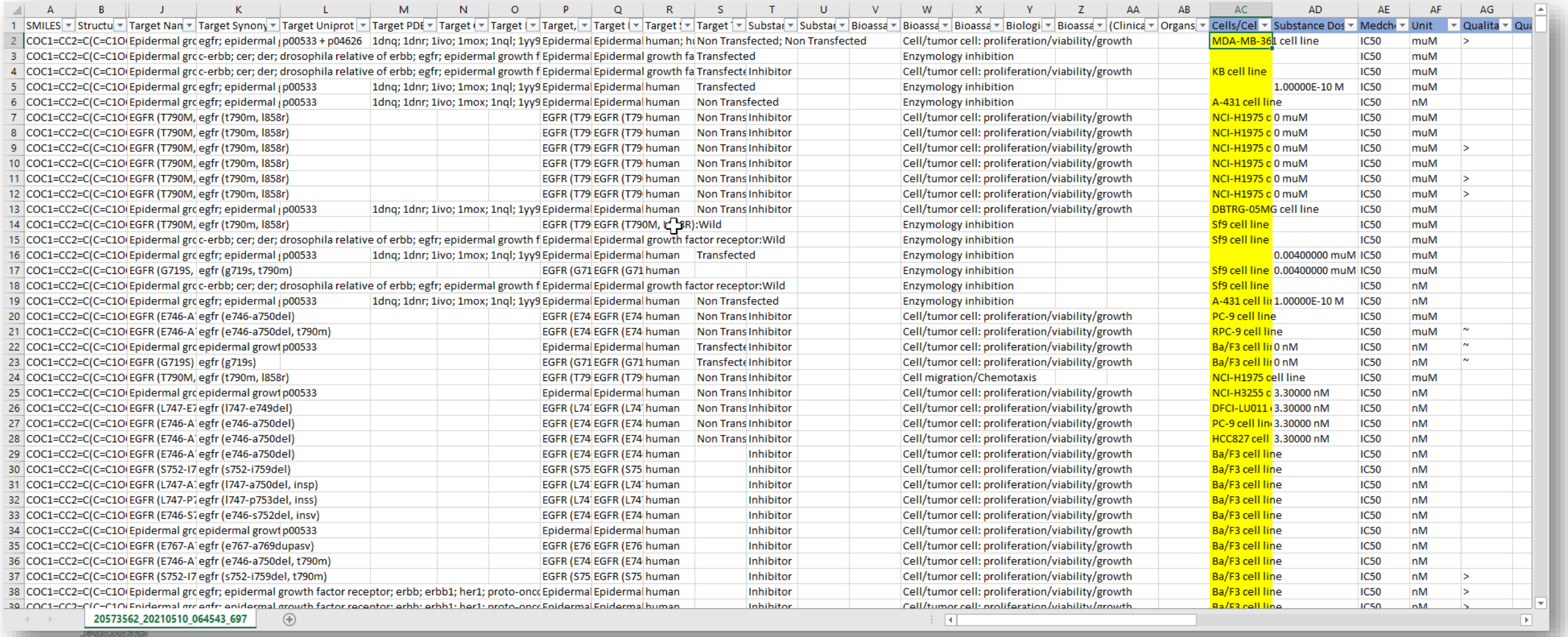
导出药化数据筛选-跨文献处理数据

- 导出表格只需要进行简单整理保留最关键信息即可

例如通过‘cell line’进行筛选，把同类型细胞系数据归类



	A	B	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG
1	SMILES	Structu	Target Nan	Target Synony	Target Uniprot	Target PDE	Target (	Target (	Target,	Target (	Target :	Target '	Substar	Substar	Bioassa	Bioassa	Bioassa	Biologi	Bioassa	(Clinica	Organs	Cells/Cel	Substance Dos	Medch	Unit	Qualita	Qua
2	COC1=CC2=C(C=C1O	Epidermal gro	egfr; epidermal	p00533 + p04626	1dnq; 1dnr; 1ivo; 1mox; 1nql; 1yy9	Epidermal	Epidermal	human; h	Non Transfected; Non Transfected		Cell/tumor cell: proliferation/viability/growth											MDA-MB-361	cell line	IC50	muM	>	
3	COC1=CC2=C(C=C1O	Epidermal gro	c-erbb; cer; der; drosophila relative of erbb; egfr; epidermal growth f			Epidermal	Epidermal growth fa	Transfected			Enzymology inhibition													IC50	muM		
4	COC1=CC2=C(C=C1O	Epidermal gro	c-erbb; cer; der; drosophila relative of erbb; egfr; epidermal growth f			Epidermal	Epidermal growth fa	Transfecte	Inhibitor		Cell/tumor cell: proliferation/viability/growth											KB cell line		IC50	muM		
5	COC1=CC2=C(C=C1O	Epidermal gro	egfr; epidermal	p00533	1dnq; 1dnr; 1ivo; 1mox; 1nql; 1yy9	Epidermal	Epidermal	human	Transfected		Enzymology inhibition												1.00000E-10 M	IC50	muM		
6	COC1=CC2=C(C=C1O	Epidermal gro	egfr; epidermal	p00533	1dnq; 1dnr; 1ivo; 1mox; 1nql; 1yy9	Epidermal	Epidermal	human	Non Transfected		Enzymology inhibition											A-431 cell line		IC50	nM		
7	COC1=CC2=C(C=C1O	EGFR (T790M,	egfr (t790m, l858r)						EGFR (T79	EGFR (T79	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						NCI-H1975 c	0 muM	IC50	muM		
8	COC1=CC2=C(C=C1O	EGFR (T790M,	egfr (t790m, l858r)						EGFR (T79	EGFR (T79	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						NCI-H1975 c	0 muM	IC50	muM		
9	COC1=CC2=C(C=C1O	EGFR (T790M,	egfr (t790m, l858r)						EGFR (T79	EGFR (T79	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						NCI-H1975 c	0 muM	IC50	muM	>	
10	COC1=CC2=C(C=C1O	EGFR (T790M,	egfr (t790m, l858r)						EGFR (T79	EGFR (T79	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						NCI-H1975 c	0 muM	IC50	muM		
11	COC1=CC2=C(C=C1O	EGFR (T790M,	egfr (t790m, l858r)						EGFR (T79	EGFR (T79	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						NCI-H1975 c	0 muM	IC50	muM	>	
12	COC1=CC2=C(C=C1O	EGFR (T790M,	egfr (t790m, l858r)						EGFR (T79	EGFR (T79	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						NCI-H1975 c	0 muM	IC50	muM	>	
13	COC1=CC2=C(C=C1O	Epidermal gro	egfr; epidermal	p00533	1dnq; 1dnr; 1ivo; 1mox; 1nql; 1yy9	Epidermal	Epidermal	human	Non Trans	Inhibitor	Cell/tumor cell: proliferation/viability/growth											DBTRG-05MG	cell line	IC50	muM		
14	COC1=CC2=C(C=C1O	EGFR (T790M,	egfr (t790m, l858r)						EGFR (T79	EGFR (T790M, | R):Wild					Enzymology inhibition						Sf9 cell line		IC50	muM		
15	COC1=CC2=C(C=C1O	Epidermal gro	c-erbb; cer; der; drosophila relative of erbb; egfr; epidermal growth f			Epidermal	Epidermal growth factor receptor:Wild				Enzymology inhibition											Sf9 cell line		IC50	muM		
16	COC1=CC2=C(C=C1O	Epidermal gro	egfr; epidermal	p00533	1dnq; 1dnr; 1ivo; 1mox; 1nql; 1yy9	Epidermal	Epidermal	human	Transfected		Enzymology inhibition												0.00400000 muM	IC50	muM		
17	COC1=CC2=C(C=C1O	EGFR (G719S,	egfr (g719s, t790m)						EGFR (G71	EGFR (G71	human					Enzymology inhibition						Sf9 cell line	0.00400000 muM	IC50	muM		
18	COC1=CC2=C(C=C1O	Epidermal gro	c-erbb; cer; der; drosophila relative of erbb; egfr; epidermal growth f			Epidermal	Epidermal growth factor receptor:Wild				Enzymology inhibition											Sf9 cell line		IC50	nM		
19	COC1=CC2=C(C=C1O	Epidermal gro	egfr; epidermal	p00533	1dnq; 1dnr; 1ivo; 1mox; 1nql; 1yy9	Epidermal	Epidermal	human	Non Transfected		Enzymology inhibition											A-431 cell li	1.00000E-10 M	IC50	nM		
20	COC1=CC2=C(C=C1O	EGFR (E746-A	egfr (e746-a750del)						EGFR (E74	EGFR (E74	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						PC-9 cell line		IC50	muM		
21	COC1=CC2=C(C=C1O	EGFR (E746-A	egfr (e746-a750del, t790m)						EGFR (E74	EGFR (E74	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						RPC-9 cell line		IC50	muM	~	
22	COC1=CC2=C(C=C1O	Epidermal gro	epidermal growt	p00533					Epidermal	Epidermal	human	Transfecte	Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell li	0 nM	IC50	nM	~	
23	COC1=CC2=C(C=C1O	EGFR (G719S)	egfr (g719s)						EGFR (G71	EGFR (G71	human	Transfecte	Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell li	0 nM	IC50	nM	~	
24	COC1=CC2=C(C=C1O	EGFR (T790M,	egfr (t790m, l858r)						EGFR (T79	EGFR (T79	human	Non Trans	Inhibitor			Cell migration/Chemotaxis						NCI-H1975 c	ell line	IC50	muM		
25	COC1=CC2=C(C=C1O	Epidermal gro	epidermal growt	p00533					Epidermal	Epidermal	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						NCI-H3255 c	3.30000 nM	IC50	nM		
26	COC1=CC2=C(C=C1O	EGFR (L747-E7	egfr (l747-e749del)						EGFR (L74	EGFR (L74	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						DFCI-LU011	3.30000 nM	IC50	nM		
27	COC1=CC2=C(C=C1O	EGFR (E746-A	egfr (e746-a750del)						EGFR (E74	EGFR (E74	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						PC-9 cell lin	3.30000 nM	IC50	nM		
28	COC1=CC2=C(C=C1O	EGFR (E746-A	egfr (e746-a750del)						EGFR (E74	EGFR (E74	human	Non Trans	Inhibitor			Cell/tumor cell: proliferation/viability/growth						HCC827 cell	3.30000 nM	IC50	nM		
29	COC1=CC2=C(C=C1O	EGFR (E746-A	egfr (e746-a750del)						EGFR (E74	EGFR (E74	human		Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		
30	COC1=CC2=C(C=C1O	EGFR (S752-I7	egfr (s752-i759del)						EGFR (S75	EGFR (S75	human		Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		
31	COC1=CC2=C(C=C1O	EGFR (L747-A	egfr (l747-a750del, insp)						EGFR (L74	EGFR (L74	human		Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		
32	COC1=CC2=C(C=C1O	EGFR (L747-P	egfr (l747-p753del, inss)						EGFR (L74	EGFR (L74	human		Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		
33	COC1=CC2=C(C=C1O	EGFR (E746-S	egfr (e746-s752del, insv)						EGFR (E74	EGFR (E74	human		Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		
34	COC1=CC2=C(C=C1O	Epidermal gro	epidermal growt	p00533					Epidermal	Epidermal	human		Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		
35	COC1=CC2=C(C=C1O	EGFR (E767-A	egfr (e767-a769dupasv)						EGFR (E76	EGFR (E76	human		Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		
36	COC1=CC2=C(C=C1O	EGFR (E746-A	egfr (e746-a750del, t790m)						EGFR (E74	EGFR (E74	human		Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		
37	COC1=CC2=C(C=C1O	EGFR (S752-I7	egfr (s752-i759del, t790m)						EGFR (S75	EGFR (S75	human		Inhibitor			Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	
38	COC1=CC2=C(C=C1O	Epidermal gro	egfr; epidermal growth factor receptor; erbb; erbb1; her1; proto-onc			Epidermal	Epidermal	human			Inhibitor					Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	
39	COC1=CC2=C(C=C1O	Epidermal gro	egfr; epidermal growth factor receptor; erbb; erbb1; her1; proto-onc			Epidermal	Epidermal	human			Inhibitor					Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	

20573562_20210510_064543_697

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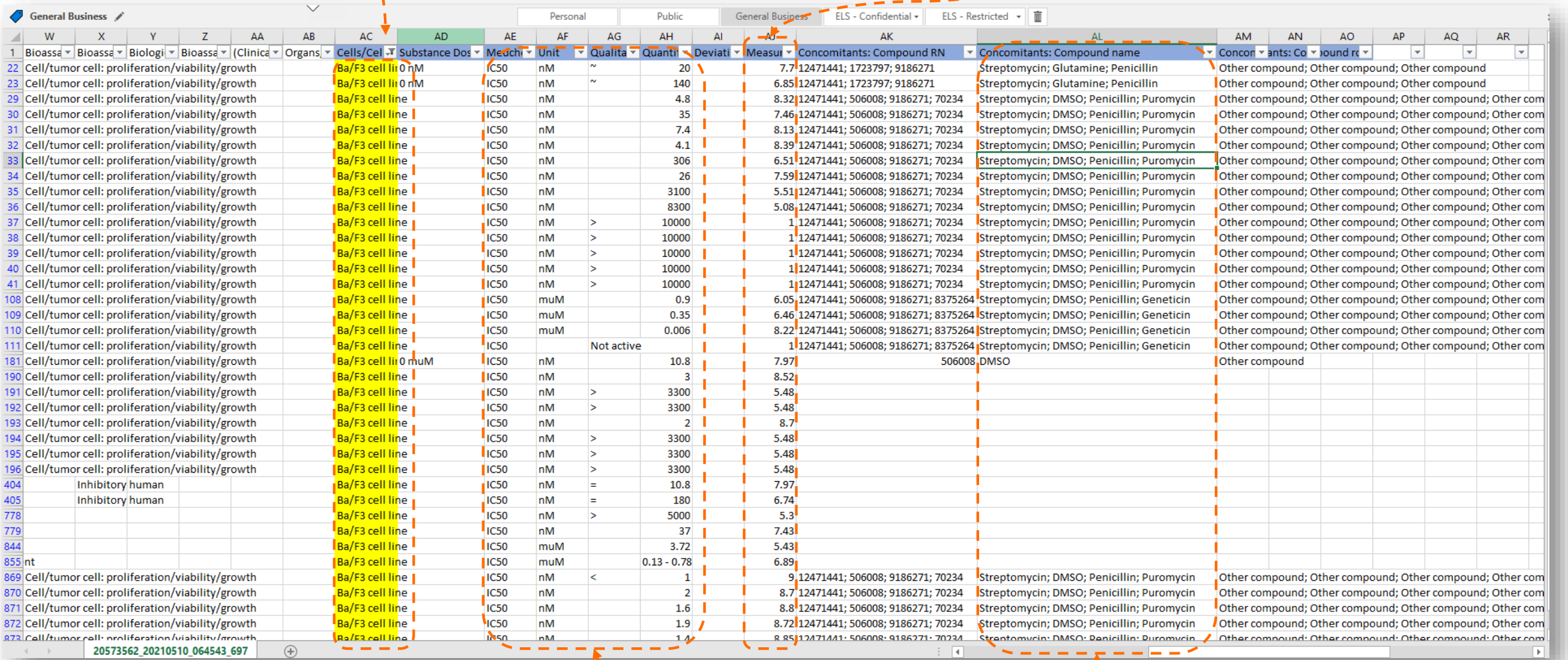
同细胞系靶点测试数据

原始数据负对数结果统一单位‘摩尔’
通过数学公式可转化为‘摩尔单位原始数据’



	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR
1	Bioassa	Bioassa	Biologi	Bioassa	(Clinica	Organs	Cells/Cel	Substance Dos	Meachi	Unit	Qualita	Quanti	Deviati	Measur	Concomitants: Compound RN	Concomitants: Compound name	Concon	ants: Co	ound rc			
22	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell li	0 nM	IC50	nM	~	20		7.7	12471441; 1723797; 9186271	Streptomycin; Glutamine; Penicillin	Other compound; Other compound; Other compound					
23	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell li	0 nM	IC50	nM	~	140		6.85	12471441; 1723797; 9186271	Streptomycin; Glutamine; Penicillin	Other compound; Other compound; Other compound					
29	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		4.8		8.32	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
30	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		35		7.46	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
31	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		7.4		8.13	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
32	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		4.1		8.39	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
33	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		306		6.51	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
34	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		26		7.59	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
35	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		3100		5.51	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
36	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		8300		5.08	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
37	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	10000		1	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
38	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	10000		1	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
39	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	10000		1	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
40	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	10000		1	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
41	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	10000		1	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
108	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	muM		0.9		6.05	12471441; 506008; 9186271; 8375264	Streptomycin; DMSO; Penicillin; Geneticin	Other compound; Other compound; Other compound; Other com					
109	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	muM		0.35		6.46	12471441; 506008; 9186271; 8375264	Streptomycin; DMSO; Penicillin; Geneticin	Other compound; Other compound; Other compound; Other com					
110	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	muM		0.006		8.22	12471441; 506008; 9186271; 8375264	Streptomycin; DMSO; Penicillin; Geneticin	Other compound; Other compound; Other compound; Other com					
111	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50		Not active			1	12471441; 506008; 9186271; 8375264	Streptomycin; DMSO; Penicillin; Geneticin	Other compound; Other compound; Other compound; Other com					
181	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell li	0 muM	IC50	nM		10.8		7.97	506008	DMSO	Other compound					
190	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		3		8.52								
191	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	3300		5.48								
192	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	3300		5.48								
193	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		2		8.7								
194	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	3300		5.48								
195	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	3300		5.48								
196	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	>	3300		5.48								
404		Inhibitory	human				Ba/F3 cell line		IC50	nM	=	10.8		7.97								
405		Inhibitory	human				Ba/F3 cell line		IC50	nM	=	180		6.74								
778							Ba/F3 cell line		IC50	nM	>	5000		5.3								
779							Ba/F3 cell line		IC50	nM		37		7.43								
844							Ba/F3 cell line		IC50	muM		3.72		5.43								
855	nt						Ba/F3 cell line		IC50	muM		0.13 - 0.78		6.89								
869	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM	<	1		9	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
870	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		2		8.7	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
871	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		1.6		8.8	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					
872	Cell/tumor cell: proliferation/viability/growth						Ba/F3 cell line		IC50	nM		1.9		8.72	12471441; 506008; 9186271; 70234	Streptomycin; DMSO; Penicillin; Puromycin	Other compound; Other compound; Other compound; Other com					

不同单位的原始数据

测试条件的基本整理
（根据原文内容整理）

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Reaxys药化数据检索-药代动力学

Reaxys

Quick search | Query builder | Results | Synthesis planner | History | Alerts

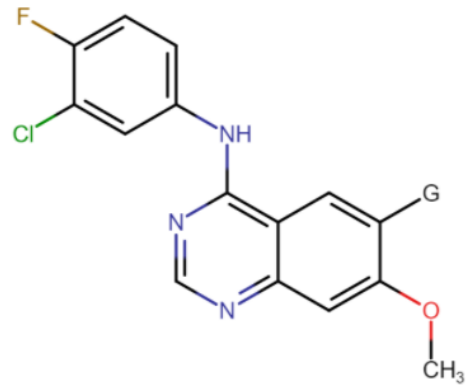
Peng Wu

Search in: Reactions > | Targets > | Substances > | Documents >

Import | Save | Reset form | Delete all

Patent Assignee | Structure | Molecular Formula | CAS RN | TI, AB & KW

Structure



As drawn

AND

Measurement Parameter contains pharmacokinetic parameters

跨文献比较，改构对药代的影响

Search fields

Fields | Forms | History

Reaxys

Topics and Keywords

Identification

Physical Properties

Spectra

MedChem

Other

Reactions

Bibliography

PubChem

Commercial Substances

eMolecules

SigmaAldrich

Structure

Advanced

Feedback

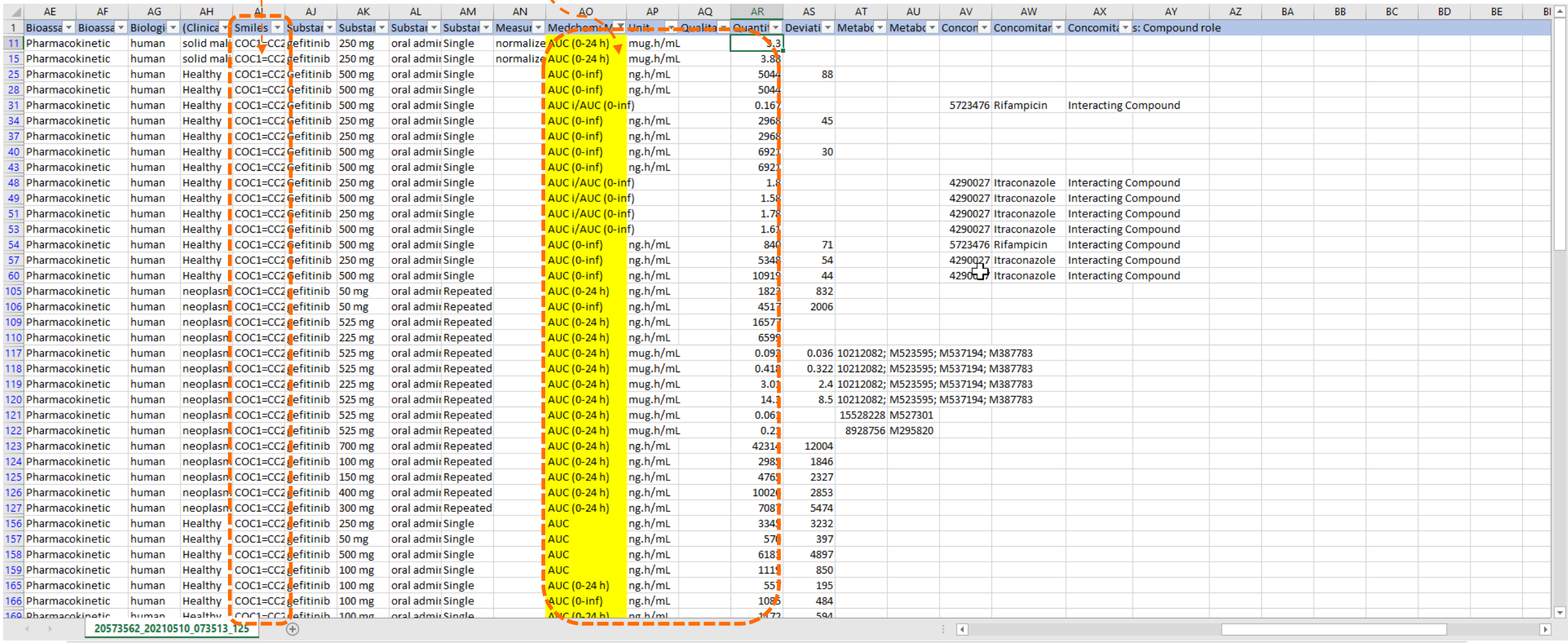
https://www.reaxys.com

ELSEVIER

同样经过简单整理就可以获得特定的药代数据

结构式

药代数据：AUC



	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY
1	Bioassa	Bioassa	Biologi	(Clinica	Smiles	Substar	Substar	Substar	Substar	Measur	Medchem	Unit	Qualita	Quanti	Deviati	Metabo	Metabo	Concon	Concomitar	Concomita	s: Compound role
11	Pharmacokinetic	human	solid mal	COC1=CC2	gefitinib	250 mg	oral admi	Single		normalize	AUC (0-24 h)	mug.h/mL		3.3							
15	Pharmacokinetic	human	solid mal	COC1=CC2	gefitinib	250 mg	oral admi	Single		normalize	AUC (0-24 h)	mug.h/mL		3.88							
25	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		5044	88						
28	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		5044							
31	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC i/AUC (0-inf)			0.167				5723476	Rifampicin	Interacting Compound	
34	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	250 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		2968	45						
37	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	250 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		2968							
40	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		6921	30						
43	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		6921							
48	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	250 mg	oral admi	Single			AUC i/AUC (0-inf)			1.8				4290027	Itraconazole	Interacting Compound	
49	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC i/AUC (0-inf)			1.58				4290027	Itraconazole	Interacting Compound	
51	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	250 mg	oral admi	Single			AUC i/AUC (0-inf)			1.78				4290027	Itraconazole	Interacting Compound	
53	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC i/AUC (0-inf)			1.61				4290027	Itraconazole	Interacting Compound	
54	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		840	71			5723476	Rifampicin	Interacting Compound	
57	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	250 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		5348	54			4290027	Itraconazole	Interacting Compound	
60	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		10919	44			4290027	Itraconazole	Interacting Compound	
105	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	50 mg	oral admi	Repeated			AUC (0-24 h)	ng.h/mL		1823	832						
106	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	50 mg	oral admi	Repeated			AUC (0-inf)	ng.h/mL		4517	2006						
109	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	525 mg	oral admi	Repeated			AUC (0-24 h)	ng.h/mL		16577							
110	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	225 mg	oral admi	Repeated			AUC (0-24 h)	ng.h/mL		6599							
117	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	525 mg	oral admi	Repeated			AUC (0-24 h)	mug.h/mL		0.093	0.036	10212082;	M523595; M537194; M387783				
118	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	525 mg	oral admi	Repeated			AUC (0-24 h)	mug.h/mL		0.418	0.322	10212082;	M523595; M537194; M387783				
119	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	225 mg	oral admi	Repeated			AUC (0-24 h)	mug.h/mL		3.01	2.4	10212082;	M523595; M537194; M387783				
120	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	525 mg	oral admi	Repeated			AUC (0-24 h)	mug.h/mL		14.3	8.5	10212082;	M523595; M537194; M387783				
121	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	525 mg	oral admi	Repeated			AUC (0-24 h)	mug.h/mL		0.063		15528228	M527301				
122	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	525 mg	oral admi	Repeated			AUC (0-24 h)	mug.h/mL		0.21		8928756	M295820				
123	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	700 mg	oral admi	Repeated			AUC (0-24 h)	ng.h/mL		42314	12004						
124	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	100 mg	oral admi	Repeated			AUC (0-24 h)	ng.h/mL		2985	1846						
125	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	150 mg	oral admi	Repeated			AUC (0-24 h)	ng.h/mL		4765	2327						
126	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	400 mg	oral admi	Repeated			AUC (0-24 h)	ng.h/mL		10026	2853						
127	Pharmacokinetic	human	neoplasn	COC1=CC2	gefitinib	300 mg	oral admi	Repeated			AUC (0-24 h)	ng.h/mL		7081	5474						
156	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	250 mg	oral admi	Single			AUC	ng.h/mL		3345	3232						
157	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	50 mg	oral admi	Single			AUC	ng.h/mL		570	397						
158	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	500 mg	oral admi	Single			AUC	ng.h/mL		6183	4897						
159	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	100 mg	oral admi	Single			AUC	ng.h/mL		1119	850						
165	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	100 mg	oral admi	Single			AUC (0-24 h)	ng.h/mL		557	195						
166	Pharmacokinetic	human	Healthy	COC1=CC2	gefitinib	100 mg	oral admi	Single			AUC (0-inf)	ng.h/mL		1086	484						
169	Pharmacokinetic	human	Healthy	COC1=CC1	gefitinib	100 mg	oral admi	Single			AUC (0-24 h)	ng.h/mL		1672	594						

20573562_20210510_073513_125

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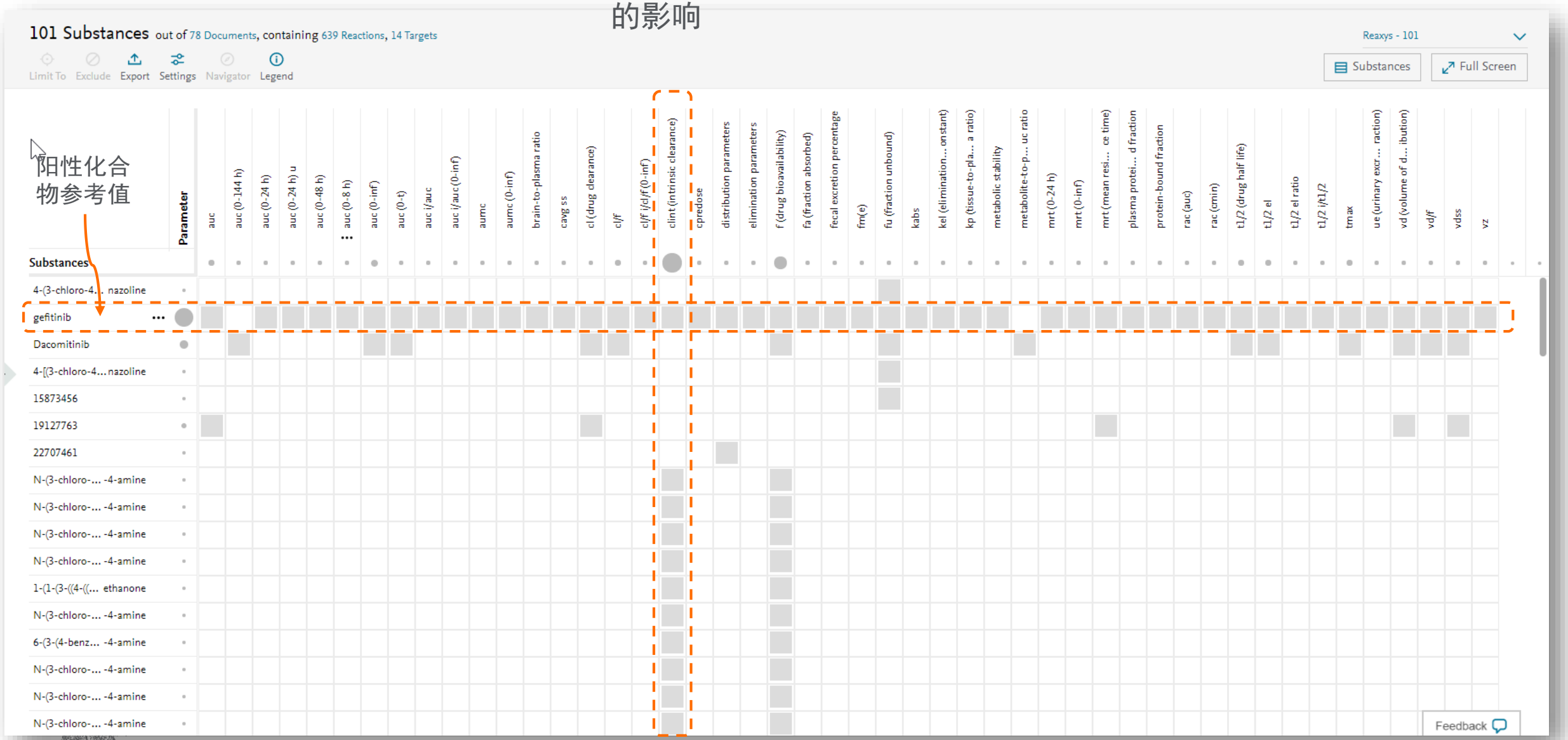
也可以横向比较，结构-药代关系

改构对清除率的影响



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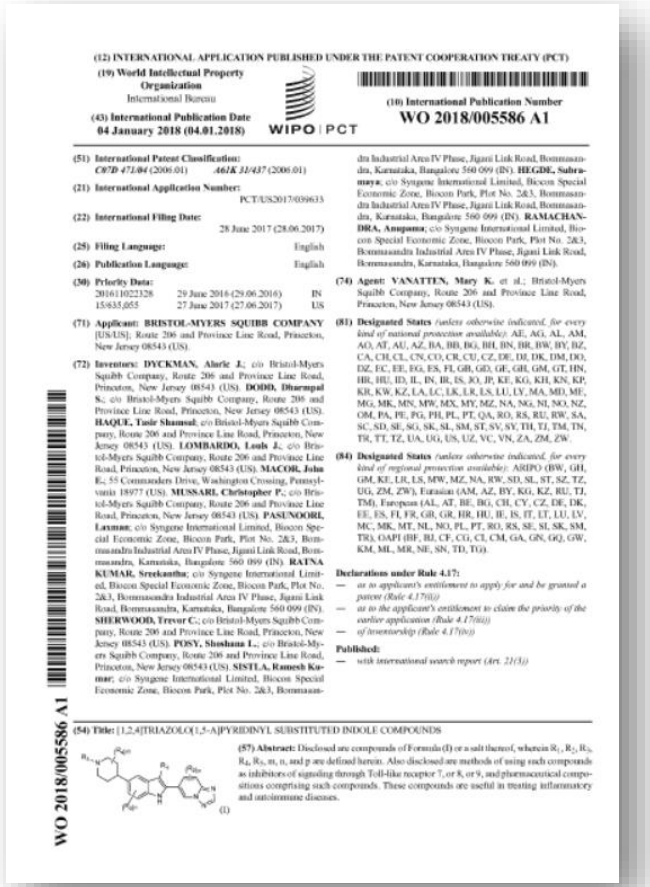
Reaxys数据+第三方软件（Spotfire）对专利进行分析

一项专利（WO2018005586（A1）已由BMS发布，包括1000+个分子（900+个具有IC50数据）作为TLR7/8/9抑制剂。对于该研究领域的竞争对手来说，分析数据以找出优化这些分子的生物活性的潜在策略以及可能成为先导化合物的关键分子是很有价值的。



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(71) Applicant: **BRISTOL-MYERS SQUIBB COMPANY** [US/US]; Route 206 and Province Line Road, Princeton, New Jersey 08543 (US).

(72) Inventors: **DYCKMAN, Alaric J.**; c/o Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, New Jersey 08543 (US). **DODD, Dharmpal S.**; c/o Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, New Jersey 08543 (US). **HAQUE, Tasir Shamsul**; c/o Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, New Jersey 08543 (US). **LOMBARDO, Louis J.**; c/o Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, New Jersey 08543 (US). **MACOR, John E.**; 55 Commanders Drive, Washington Crossing, Pennsylvania 18977 (US). **MUSSARI, Christopher P.**; c/o Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, New Jersey 08543 (US). **PASUNOORI, Laxman**; c/o Syngene International Limited, Biocon Special Economic Zone, Biocon Park, Plot No. 2&3, Bommasandra Industrial Area IV Phase, Jigani Link Road, Bommasandra, Karnataka, Bangalore 560 099 (IN). **RATNA KUMAR, Sreekantha**; c/o Syngene International Limited, Biocon Special Economic Zone, Biocon Park, Plot No. 2&3, Bommasandra Industrial Area IV Phase, Jigani Link Road, Bommasandra, Karnataka, Bangalore 560 099 (IN). **SHERWOOD, Trevor C.**; c/o Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, New Jersey 08543 (US). **POSY, Shoshana L.**; c/o Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, New Jersey 08543 (US). **SISTLA, Ramesh Kumar**; c/o Syngene International Limited, Biocon Special Economic Zone, Biocon Park, Plot No. 2&3, Bommasandra Industrial Area IV Phase, Jigani Link Road, Bommasandra, Karnataka, Bangalore 560 099 (IN). **HEGDE, Subramaya**; c/o Syngene International Limited, Biocon Special Economic Zone, Biocon Park, Plot No. 2&3, Bommasandra Industrial Area IV Phase, Jigani Link Road, Bommasandra, Karnataka, Bangalore 560 099 (IN). **RAMACHANDRA, Anupama**; c/o Syngene International Limited, Biocon Special Economic Zone, Biocon Park, Plot No. 2&3, Bommasandra Industrial Area IV Phase, Jigani Link Road, Bommasandra, Karnataka, Bangalore 560 099 (IN).

(74) Agent: **VANATTEN, Mary K.** et al.; Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, New Jersey 08543 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
— *of inventorship (Rule 4.17(iv))*

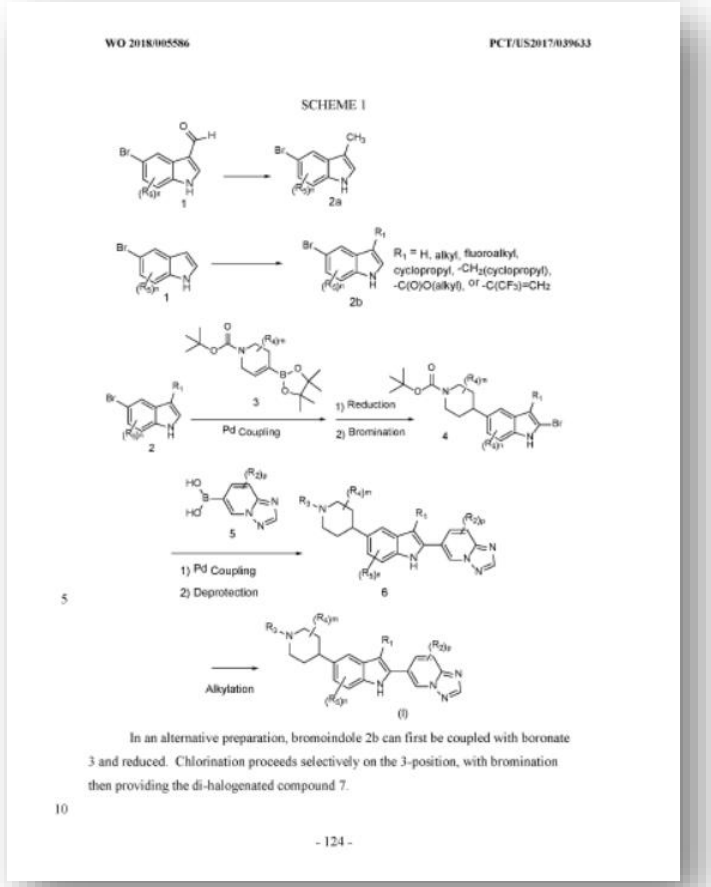
Published:
— *with international search report (Art. 21(3))*

(54) Title: [1,2,4]TRIAZOLO[1,5-A]PYRIDINYL SUBSTITUTED INDOLE COMPOUNDS

(57) Abstract: Disclosed are compounds of Formula (I) or a salt thereof, wherein R_1, R_2, R_3, R_4, R_5, m, n, and p are defined herein. Also disclosed are methods of using such compounds as inhibitors of signaling through Toll-like receptor 7, or 8, or 9, and pharmaceutical compositions comprising such compounds. These compounds are useful in treating inflammatory and autoimmune diseases.

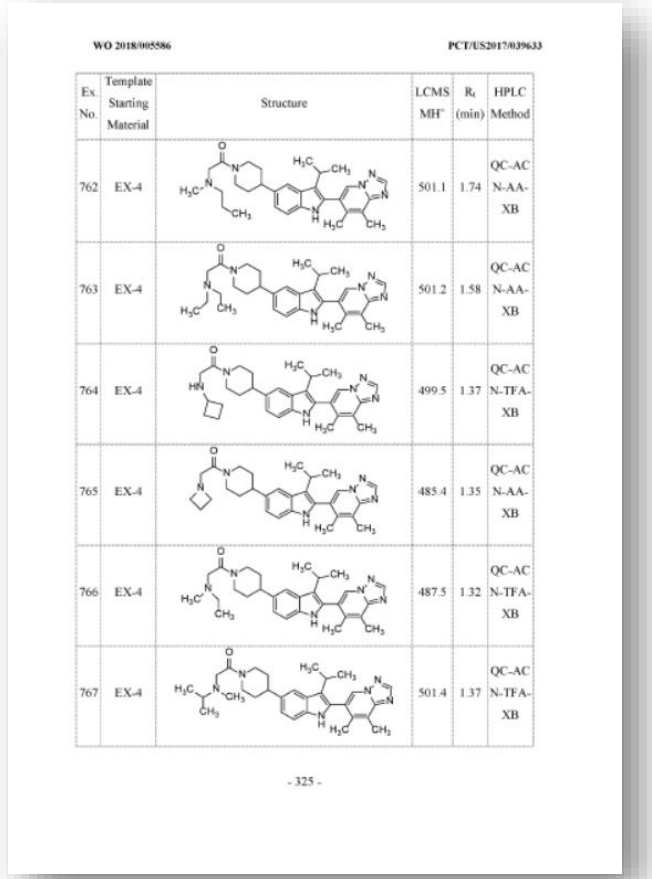
(I)

WO 2018/005586 A1



SCHEME 1

In an alternative preparation, bromoindole 2b can first be coupled with boronate 3 and reduced. Chlorination proceeds selectively on the 3-position, with bromination then providing the di-halogenated compound 7.



Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
762	EX-4		501.1	1.74	QC-AC N-AA-XB
763	EX-4		501.2	1.58	QC-AC N-AA-XB
764	EX-4		499.5	1.37	QC-AC N-TFA-XB
765	EX-4		485.4	1.35	QC-AC N-AA-XB
766	EX-4		487.5	1.32	QC-AC N-TFA-XB
767	EX-4		501.4	1.37	QC-AC N-TFA-XB

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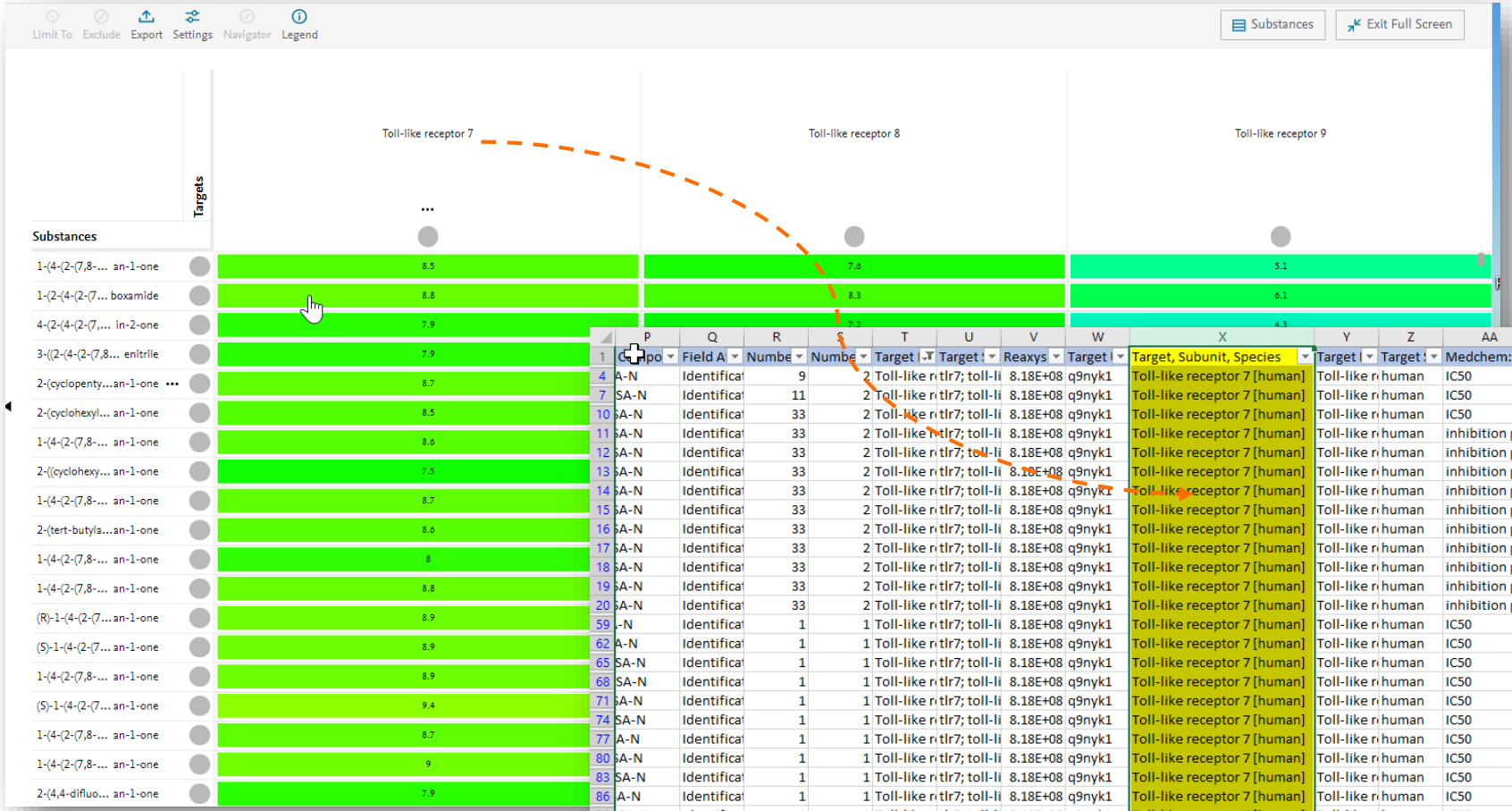
Reaxys已经对数据进行整理，以及初步标准化



整理后的TL7数据

	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK
1	Compo	Field A	Numbe	Numbe	Target	Target	Reaxys	Target	Target, Subunit, Species	Target	Target	Medchem: M	Unit	Qualita	Quanti	Deviati	Statisti	Measur	Measur	Measur	Statisti	Measur
4	A-N	Identificat	9	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		0.5							9.3
7	SA-N	Identificat	11	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		0.3							9.52
10	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1.4							8.85
11	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		18			Interleukin-6				
12	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		49			Interleukin-6				
13	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		65			Interleukin-6				
14	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		84			Interleukin-6				
15	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		91			Interleukin-6				
16	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		11			Interferon alpha				
17	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		27			Interferon alpha				
18	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		62			Interferon alpha				
19	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		88			Interferon alpha				
20	SA-N	Identificat	33	2	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	inhibition perc	%		99			Interferon alpha				
59	-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		2.9							8.54
62	A-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1.4							8.85
65	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		11.6							7.94
68	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		10.7							7.97
71	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1.7							8.77
74	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		3							8.52
77	A-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		2.2							8.66
80	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		27.4							7.56
83	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1.7							8.77
86	A-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		2.3							8.64
89	YSA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		10.1							8
92	-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1.4							8.85
95	-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1.2							8.92
98	A-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1.2							8.92
101	YSA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1.1							8.96
104	-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		0.4							9.4
107	A-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		2							8.7
110	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1							9
113	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		12.2							7.91
116	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		1							9
119	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		0.9							9.05
122	A-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		3.7							8.43
125	YSA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		0.7							9.15
128	SA-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		4.5							8.35
131	A-N	Identificat	1	1	Toll-like r	tlr7; toll-li	8.18E+08	q9nyk1	Toll-like receptor 7 [human]	Toll-like r	human	IC50	nM		3.5							8.46

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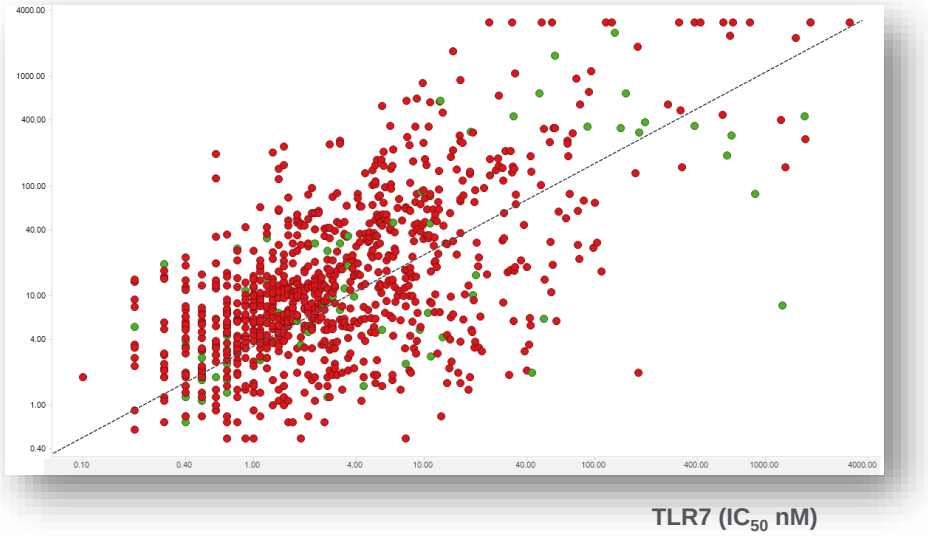
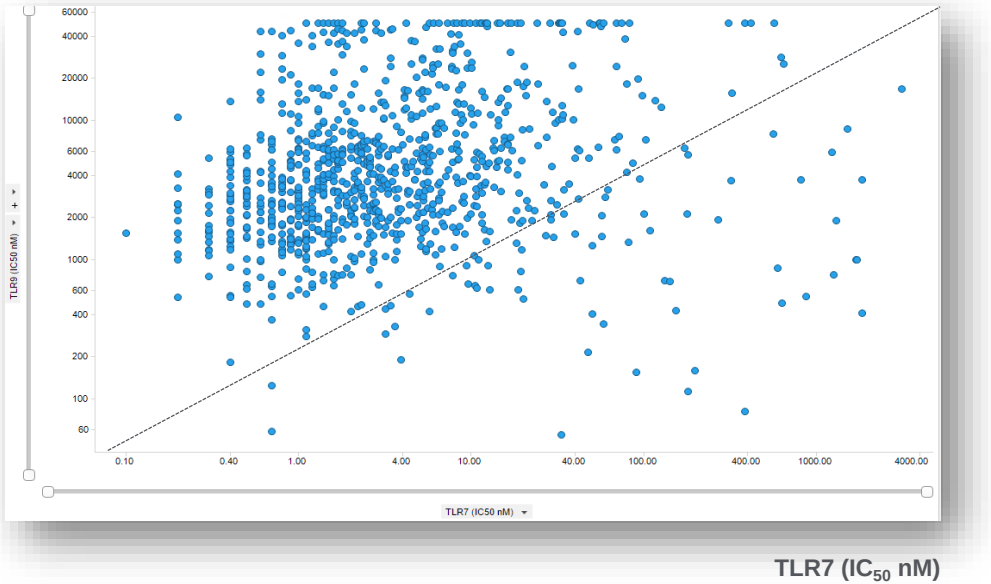
Reaxys已经对数据进行整理，通过Spotfire输出靶点选择性结果

TLR8 (IC_{50} nM)



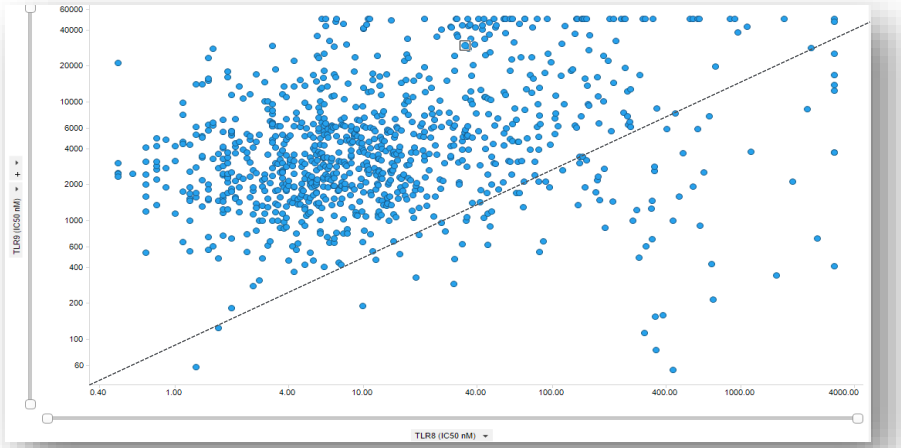
TLR7 (IC_{50} nM)

TLR9 (IC50 nM)



TLR7 (IC_{50} nM)

TLR9 (IC_{50} nM)



TLR8 (IC_{50} nM)

TLR7和TLR8之间活性数据的一致相关性。这可能意味着这些化合物可能具有抑制TLR7和8的药效团结构

Interactive Visualization in Spotfire

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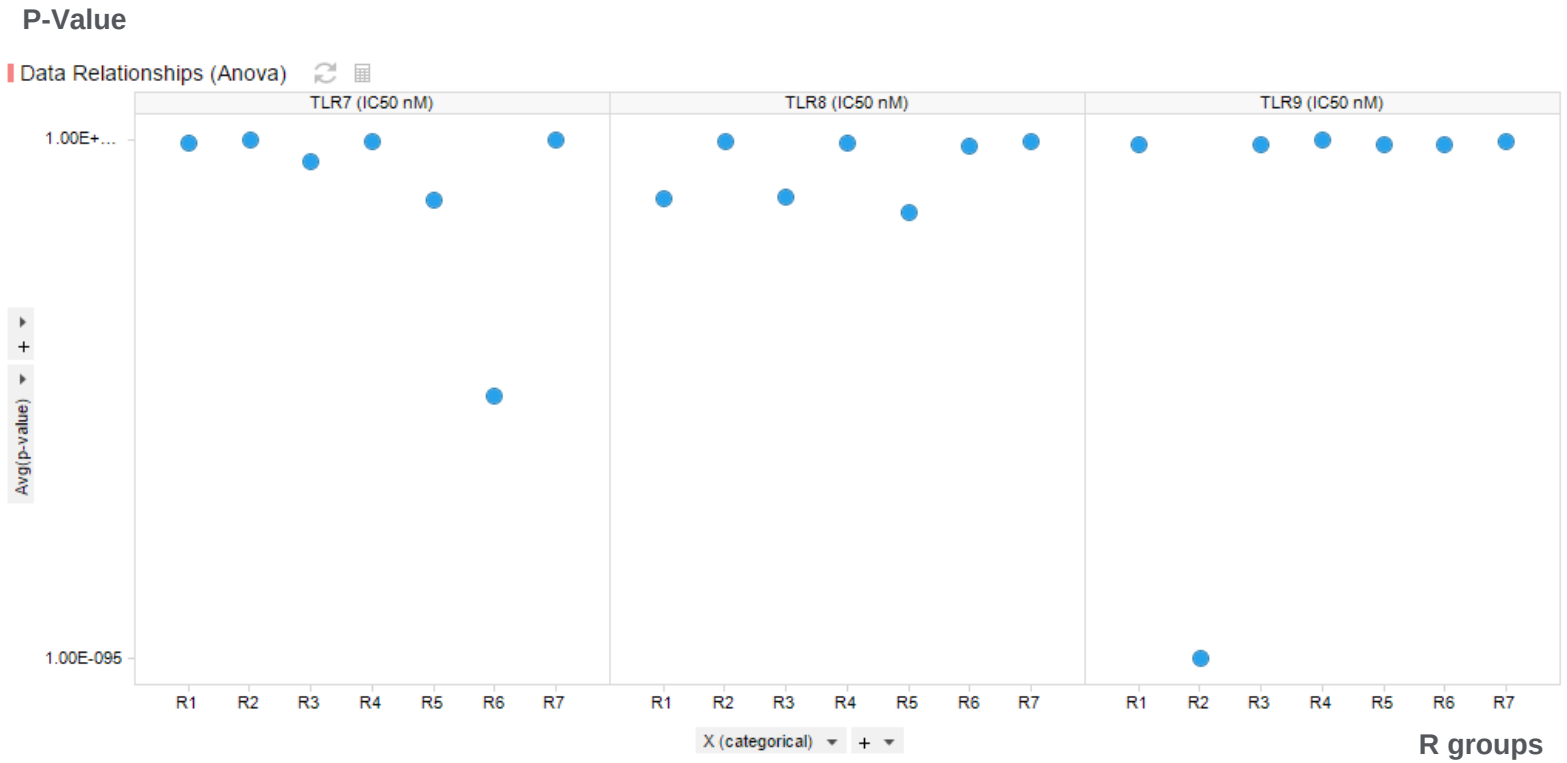
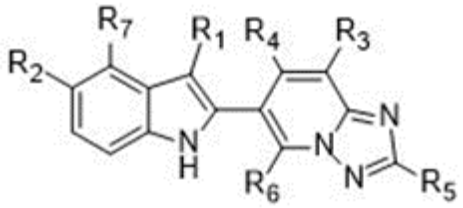
Reaxys已经对数据进行整理，通过Spotfire输出R-goup方差分析





R2, R6 and R5 is the most key R group to the inhibition activities of TLR7, 8 and 9, respectively.

IC50数据与R组数据关系的方差分析

Y (numerical)	X (categorical)	p-value
TLR9 (IC50 nM)	R2	1.27E-95
TLR7 (IC50 nM)	R6	1.07E-47
TLR8 (IC50 nM)	R5	3.89E-14

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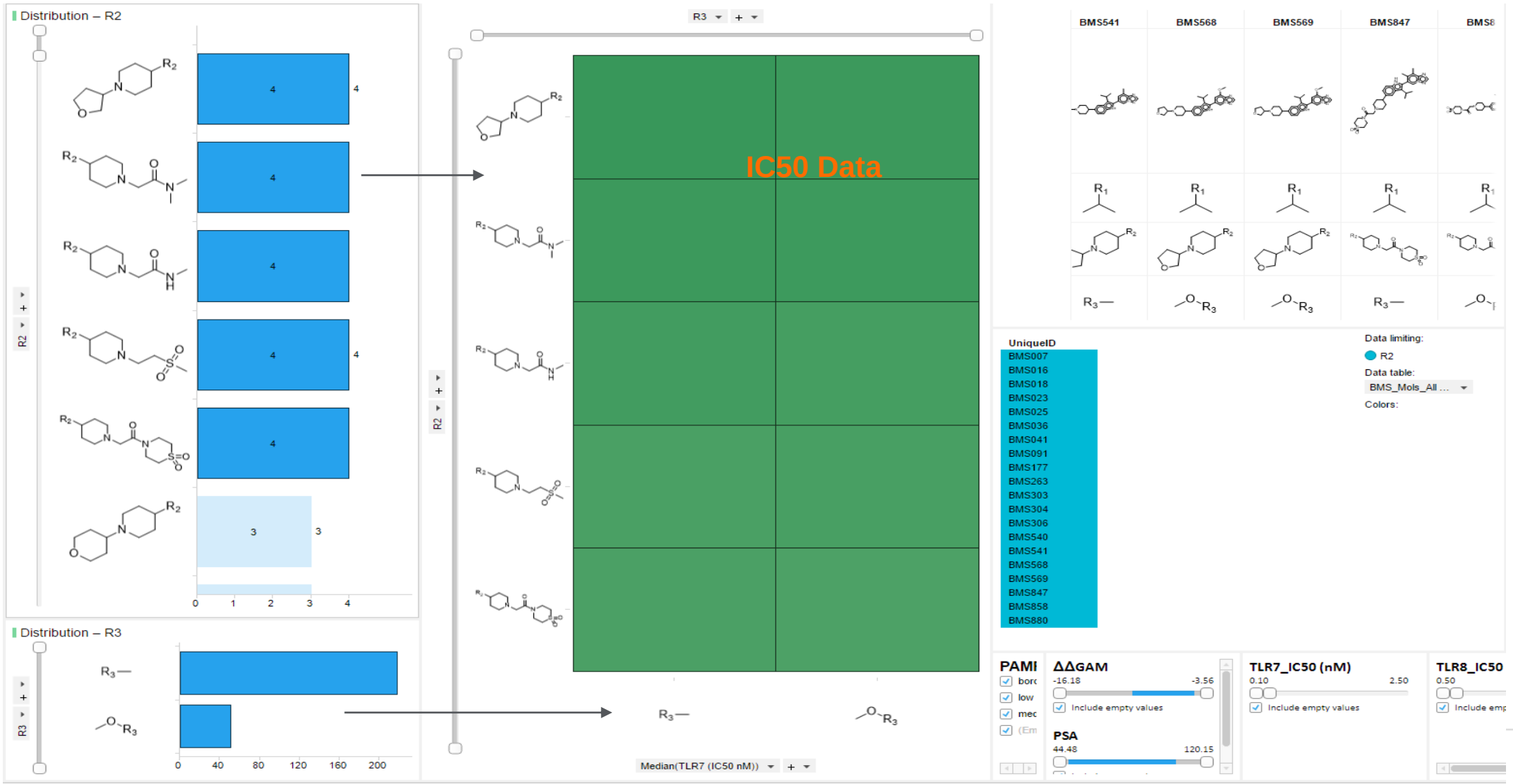
Interactive Visualization in Spotfire

Reaxys已经对数据进行整理，通过Spotfire输出IC50构效结果



科学家可以通过考虑R基团和IC50数据来提取关键化合物

Interactive Visualization in Spotfire

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Thank you